

**REMARKS**

Claims 28-82 are all the claims pending in the application. Each of the claims has been rejected.

Upon entry of this Amendment, claims 58, 60 and 68-69 will be canceled, and claims 28-57, 59, 61-67 and 70-82 will be pending.

Claim 28 has been amended to include the subject matter of claim 36.

Claim 46 has been amended to include the subject matter of claims 58 and 60.

Claim 67 has been amended to include the subject matter of claims 68-69.

No new matter has been added. Entry of the Amendment is respectfully requested.

**I. Claim Rejections Under 35 U.S.C. §112**

At paragraph 3 of the Office Action, claims 28-82 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite.

The Examiner states that the terms “biomolecules”, “electromagnetic radiation”, and “an extrinsic fluorescent marker”, and the phrase “an extrinsic fluorescent marker is not part of the system”, are vague and indefinite.

Applicants note that a definition for the term “biomolecule” is provided in paragraph [0063] of the specification. As the term is specifically defined in the specification, it is not indefinite. However, to further prosecution of this application, the claims have been amended to recite specific biomolecules.

The skilled artisan would readily understand the meaning of the term “electromagnetic radiation.” For example, the skilled artisan would understand the term to

mean radiation that contains both electric and magnetic components and that travels at the speed of light, and that examples of electromagnetic radiation include radiowaves, microwaves, infrared rays, light, ultraviolet rays, x-rays, and gamma-rays. *See, e.g.,* <http://xenon.che.ilstu.edu/genchemhelphomepage/glossary/e.html>; [http://www.nmlites.org/standards/science/glossary\\_2.htm](http://www.nmlites.org/standards/science/glossary_2.htm); [http://en.wikipedia.org/wiki/Electromagnetic\\_radiation](http://en.wikipedia.org/wiki/Electromagnetic_radiation).

The skilled artisan would likewise readily understand the plain meaning of the term “extrinsic fluorescent marker,” that is, a marker added to the system that emits light when exposed to radiation from an external source.

The skilled artisan would further readily understand the meaning of the phrase “an extrinsic fluorescent marker is not part of the system,” that is, a marker (that emits light when exposed to radiation from an external source) that is not added to the system.

In view of these comments and the amendments to the claims, Applicants respectfully request reconsideration and withdrawal of these rejections.

## **II. Claim Rejections Under 35 U.S.C. §102**

**A.** At paragraph 5 of the Office Action, claims 28-32, 37-43 and 45 are rejected under 35 U.S.C. §102(b) as being anticipated by Kummerlen et al. (1993).

The Examiner states that Kummerlen teaches enhancement of fluorescent intensity where a dye film is brought into proximity with a film on a support, with a resonant excitation phenomenon due to the collective action of the film. The Examiner further states that the situation of a film consists of many individual metal spheroids, with excitation wavelengths of

514 nm, 488 nm and 458 nm. The Examiner states that Kummerlen teaches the dye is deposited on top of a quartz layer, and maximum enhancement is observed at a distance of around 60-70 nm. The Examiner explains that because the term “biomolecules” is not defined, any molecule is interpreted as a biomolecule.

Included herewith is an amendment to claim 28 such that it recites specific biomolecules. As Kummerlen only teaches a dye and does not teach any of the recited biomolecules, Kummerlen does not teach each and every limitation of the invention as recited in claims 28-32, 37-43 and 45 and thus does not anticipate these claims under 35 U.S.C. §102(b).

Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection.

**B.** At paragraph 6 of the Office Action, claims 46-82 are rejected under 35 U.S.C. §102(b) as being anticipated by Lakowicz et al. (1999).

The Examiner states that Lakowicz teaches an assay in which a metal-ligand complex is brought into interactive proximity with an analyte in a sample, and that the mixture is irradiated with electromagnetic light energy so as to cause emission of light which indicates the analyte of interest is present in the sample. The Examiner further comments on the location of support for elements and limitations recited in the dependent claims.

Included herewith is an amendment to claims 46 and 67 such that they recite the use of six different metals in the invention. Lakowicz teaches the use of rhenium, ruthenium and osmium, none of which is recited in the amended claims. As such, Lakowicz does not teach and

every element of claims 46-82, and thus does not anticipate claims 46-82 under 35

U.S.C. §102(b).

Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection.

### **III. Claim Rejections Under 35 U.S.C. §103**

At paragraph 8 of the Office Action, claims 33-36 and 44 are rejected as being unpatentable under 35 U.S.C. §103(a) over Kummerlen in view of Lakowicz.

The Examiner states that Kummerlen does not teach the use of a second biomolecule as recited in claims 33-36 and 44, but that Lakowicz cures this deficiency. The Examiner contends that the skilled artisan would have been motivated to use a biomolecule, as taught by Lakowicz, because the metal-ligand complex works as a biomolecular probe which has high sensitivity and specificity, and is valuable in biochemistry and biophysics. The Examiner concludes that it would have been *prima facie* obvious to attach the biomolecules, such as nucleic acid or protein, to the metal-ligand particle to make the instant invention.

Applicants note that claim 33 recites the use of an oxide coating on metal particles of claim 28. As the Examiner does not specifically comment on the oxide coating, it appears that the Examiner mistakenly included it in this group of claims.

As to the remainder of the claims, Applicants respectfully assert that the Examiner has not established a *prima facie* case of obviousness. The skilled artisan would have not been motivated to combine the teachings of Kummerlen and Lakowicz, nor would the skilled artisan have had a reasonable expectation of success in doing so.

In particular, Kummerlen teaches the results of experiments designed to investigate means for enhancing fluorescent intensity of dye molecules positioned near metal films. Kummerlen observed the differences in fluorescent intensity through the use of dye molecules positioned at different distances from the films (see, e.g., Conclusion). The skilled artisan would not have been motivated to attach a biomolecule to the dye molecules of Kummerlen. Indeed, while the Examiner has stated that the skilled artisan would have done so to produce a biomolecular probe with high sensitivity and specificity that is “valuable in biochemistry and biophysics,” the Examiner does not explain why such would be the case. The Examiner has not identified any teaching of how the addition of the biomolecules to the dye molecules could improve the system of Kummerlen, or in some other manner provide a motivation to use the biomolecules in the system of Kummerlen.

The addition of a biomolecule to the dye used in Kummerlen would likely have a detrimental affect on the system of Kummerlen. As Kummerlen teaches the importance of minor changes in distance between the dye molecules and the metal films, the skilled artisan might reasonably expect that the use of biomolecules would disrupt the dye monolayers and create variability in the distance between the film and the dye molecules. Further, Applicants note that in the system that would result from the combination of the two disclosures, the dye molecule would be linked to a ligand (biomolecule)-metal complex. As a result, there would be two metal components in the system, in different locations, that would likely completely change the effect on the fluorescence emitted by the dye molecule. The Examiner does not explain why the skilled artisan would have a reasonable expectation of success in creating a functional system when each

of the components of the two cited disclosures is combined. Thus, the skilled artisan would not have had a reasonable expectation of success in combining the two disclosures.

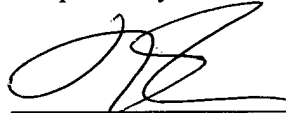
Accordingly, the Examiner has not established a *prima facie* case of obviousness and Applicants respectfully request reconsideration and withdrawal of this rejection.

#### IV. Conclusion

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,



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